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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,226	06/06/2005	Marnix L Bosch	020093-004010US	9406

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,226	BOSCH, MARNIX L	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *10-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 13-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **[1]** has been entered.

Claims 1-9, 13-32, species: 1) BCG and interferon gamma, or LPS, TNF-alpha as maturing agent, and 2) CD86 or CD80 co-stimulatory molecule are examined in the instant application.

Withdrawn Rejection

The 102 and 103 rejections have been withdrawn, in view of the amendment, and replaced with new 102 and 103 rejections.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5,13 are rejected under 35 U.S.C. 102(b) as being anticipated by Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07, and as evidenced by Labeur et al, 1999, J Immunol, 162: 168-175, of record.

Claims 1-3, 5, 13 are as followed:

1. (Currently amended) A method for producing an anti-tumor immune response comprising administration to an individual with a cancerous tumor a cell population comprising partially matured dendritic cells that have been partially matured in vitro, wherein the partially matured dendritic cells can take up and process antigen in vivo and are enabled to induce an anti-tumor immune response subsequent to administration to the individual.

2. (Original) The method according to claim 1, wherein the dendritic cells are obtained from skin, spleen, bone marrow, thymus, lymph nodes, umbilical cord blood, or peripheral blood.

3. (Original) The method according to claim 2, wherein the dendritic cells are obtained from the individual to be treated.

5. (Currently amended) The method according to claim 1, wherein the dendritic cells are partially matured in vitro in the presence of a dendritic cell maturation agent.

13. (Previously presented) The method according to claim 1, wherein the partially matured dendritic cells are administered directly into the cancerous tumor.

"Wherein the partially matured dendritic cells can take up and process antigen in vivo and are enabled to induce an anti-tumor immune response subsequent to administration to the individual" of claim 1 is reasonably interpreted as the intended results, because they simply express the intended result of a process step positively recited (MPEP 2111.04 [R-3]).

Triozzi et al teach intratumoral injection of dendritic cells (DCs) derived in vitro in patients with metastatic melanoma or breast cancer (title, abstract). Triozzi et al teach that DCs are obtained from isolated, autologous peripheral blood Mo cells that are treated with GM-CSF and IL-4 (p.2647, second column, item under Treatment). Triozzi et al further teach that DCs generated in vitro by GM-CSF and IL-4 express the co-stimulatory molecules **CD80 and CD86**, and a low number of CD83 (p.2649, first column, item under Results). Triozzi et al teach that tumor regression and tumor infiltrating lymphocytes are induced in the treated melanoma and breast cancer (p.2651, second column, paragraph under Discussion).

The DCs taught by Triozzi et al are partially matured in vitro, as evidenced by Labeur et al. Labeur et al teach that supplementing GM-CSF with IL-4 significantly enhance DCs differentiation, leading to an intermediate degree of maturation (p.173, second column, last paragraph). Labeur et al teach that DCs matured with GM-CSF plus IL-4 has the ability to pick up antigen in vitro and process said antigen in vivo (figure 3 on page 172, and figure 4 on page 173).

It is noted that DCs that are capable of pick up and process antigen are **interpreted as partially mature DCs**, as compared to those terminally matured DCs (which is called fully mature in the instant application, p.11, lines 17-18) that lose the ability to pick up and process antigen (see the instant specification, p.11, paragraph before last, concerning disclosure on partially matured DCs), regardless whether said DCs are named fully matured DCs by the art. For example, those fully mature DCs exposed to GM-CSF plus IL-4 and CD40L taught by Labeur et al (Labeur et al, abstract), that have the ability to pick up and process antigen, are interpreted as partially matured DCs.

Although the Triozzi reference does not explicitly teach that the generated DCs are partially mature, however, the claimed DCs appear to be the same as the prior art DCs. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 2, 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07, **in view of** Labeur et al, 1999, J Immunol, 162: 168-175, of record, and further in view of Murphy et al (US 5,788,963, filed on 07/31/1995, of record).

Claims 2, 4 are as follows:

2. (Original) The method according to claim 1, wherein the dendritic cells are obtained from skin, spleen, bone marrow, thymus, lymph nodes, umbilical cord blood, or peripheral blood.

4. (Original) The method according to claim 2, wherein the dendritic cells are obtained from a healthy individual HLA-matched to the individual to be treated.

The teaching of Triozzi et al, and Labeur et al has been set forth above.

Triozzi et al and Labeur et al do not teach that: 1) DCs are obtained from skin, spleen, bone marrow, thymus, lymph nodes, umbilical cord blood, and 2) DCs are obtained from a healthy individual HLA-matched to the individual to be treated.

Murphy et al teach isolation of DCs for prostate cancer therapy, where DCs are obtained from any tissue where they reside, including **the skin, the spleen, bone marrow, lymph nodes and thymus** as well as the circulatory system, including blood and lymphs (column 5, lines 54-65). Murphy et al teach that **cord blood** is another source of human DCs, where a male is born into a family known to be high risk of prostate cancer, and that said DCs can be cryopreserved for later use (column 5, lines 62-65). Murphy et al teach that DCs can be obtained from prostate cancer patient to be treated, or **from healthy individual with matched HLA** in terms of HLA antigens, because patients previously treated radiation or chemotherapy often are not able to provide sufficient or effecient DCs (column 6, lines 37-57). Murphy et al teach that CD8+ T cells, after interaction with antigen presenting cells, which express MHC class I or II molecule associated with the antigen, are sensitized and capable of killing any cells that express the specific antigen associated with matching MHC class I molecule (column 2, second paragraph). It is noted that DCs are antigen presenting cells.

It would have been prima facia obvious for one of ordinary skill in the art at the time the invention was made to obtain the DCs taught by Triozzi et al and Labeur et al from skin, spleen, bone marrow, thymus, lymph nodes, umbilical cord blood, as taught by Murphy et al, to increase the number of available sources for making DCs.

It would have been obvious to replace DCs obtained from the individual to be treated, taught by Triozzi et al and Labeur et al with DCs isolated from a healthy individual HLA-

matched to the individual to be treated as taught by Murphy et al, to increase the number of available DCs, for example, in situations where the patient to be treated cannot provide sufficient DCs, as taught by Murphy et al. Further, an HLA-matched DCs would be necessary, because antigen presentation of DCs is restricted to the complementing HLA molecule, in view of the teaching of Murphy et al.

2. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07 in view of Labeur et al, 1999, J Immunol, 162: 168-175, of record, and further in view of US 20050059151 (Bosch et al, which has as priority US 60/317592, filed on 09/06/01, of record), and Chakraborty et al, 2000, Clin Immunol, 94(2): 88-98, IDS # AF of 05/09/07, of record).

Claims 6-9 are as follows:

6. (Original) The method according to claim 5, wherein the dendritic cell maturation agent is Bacillus Calmette-Guerin (BCG), interferon gamma (IFN-gamma), lipopolysaccharide (LPS), tumor necrosis factor alpha (TNF-alpha), or any combination thereof.

7. (Original) The method according to claim 6, wherein BCG comprises whole BCG, cell wall constituents of BCG, BCG-derived lipoarabidomannans, or BCG components.

8. (Original) The method according to claim 6, wherein the BCG is heat- inactivated BCG or formalin-treated BCG.

9. (Original) The method according to claim 6, wherein the effective amount of BCG is about 10^5 to 10^7 cfu per milliliter of tissue culture media and the effective amount of IFN-gamma is about 100 to about 1000 Units per milliliter of tissue culture media.

The teaching of Triozzi et al and Labeur et al has been set forth above. Labeur et al further teach that ability of DCs to promote antitumor immunity correlates with their high efficiency of stimulating resting T cells and high production of IL-12 (p.173, second column, second paragraph).

Triozzi et al and Labeur et al do not teach the use of BCG and interferon gamma for maturing CDs. Further, Triozzi et al and Labeur et al do not teach: 1) BCG comprises whole BCG, cell wall constituents of BCG, BCG-derived lipoarabidomannans, or BCG components, 2) the BCG is heat- inactivated BCG or formalin-treated BCG, and 3) the effective amount of BCG is about 10^5 to 10^7 cfu per milliliter of tissue culture media and the effective amount of IFN-gamma is about 100 to about 1000 Units per milliliter of tissue culture media.

Bosch et al teach that maturing DCs, such as those previously exposed to GM-CSF plus IL-4, with **IFN-gamma and BCG** promotes DC production of IL-12, and reduces or inhibits production of IL-10, thereby priming the mature dendritic cells for a type 1 (Th-1) response (para 0039, claims 1, 6). Bosch et al teach that in contrast to type 1 response, type 2 response is characterized by production of more IL-10 than IL-12 and lack of induction of a CTL response (para 0022, last two lines). Bosch et al teach that: 1) effective amounts of BCG typically range from about 10.sup.5 to 10.sup.7 cfu per milliliter of tissue culture media, 2) Effective amounts of IFN.gamma typically range from about 100-1000 U per milliliter of tissue culture media (para 0038). Bosch et al teach that Bacillus Calmette-Guerin (BCG) is an avirulent strain of M bovis, and as used herein, BCG refers to whole BCG as well as cell wall constituents, BCG-derived lipoarabidomannans, and other BCG components that are associated with induction of a type 2 immune response (para 0038). Bosch et al teach that BCG is optionally inactivated, such as heat-

inactivated BCG, formalin-treated BCG, and the like (para 0038). Thus the type of BCG, and the amount of BCG and interferon gamma are the same as those of the claimed invention. Bosch et al teach that maturation of dendritic cells can be monitored by methods known in the art, such as detection of cell surface markers or cytokine production (p.0041).

Chakraborty et al teach that DCs that produce IL-12 efficiently stimulate T cells, whereas DCs that produce IL-10 are inhibitory (abstract, figure 2 on page 93). Chakraborty et al teach that DCs that produce IL-12 up-regulate the co-stimulatory CD80 and CD86 (p.91, second column, first paragraph, table 3 on page 95).

It would have been prima facia obvious for one of ordinary skill in the art at the time the invention was made to add to GM-CSF plus IL-4 maturing agent taught by Triozzi et al and Labeur et al with BCG and interferon gamma, as taught by Bosch et al, in the method taught by Triozzi et al and Labeur et al for maturing DCs in vitro for use in producing an anti-cancer response, because of the following reasons:

1) A combination of BCG and interferon gamma selectively produces more maturing DCs that secrete IL-12 than those inhibiting DCs secreting IL-10, as taught by Bosch et al,

2) DCs that secrete IL-12 efficiently stimulate T cells, whereas DCs that produce IL-10 are inhibitory, as taught by Chakraborty et al.

3) The ability of DCs to promote antitumor immunity correlates with their high efficiency of stimulating resting T cells and high production of IL-12, as taught by Labeur et al.

In other words, BCG and interferon gamma as maturing agent as taught by Bosch et al would be advantageous, because they selectively enhance the production of stimulating DCs that

secrete IL-12, and therefore efficiently stimulating T cells, in view of the teaching of Chakraborty et al, and promoting anti-tumor immunity, in view of the teaching of Labeur et al.

3. Claims 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07 in view of Labeur et al, 1999, J Immunol, 162: 168-175, of record.

The following are claims 14-18:

14. (Original) The method according to claim 1, wherein the partially matured dendritic cells are administered into a tumor bed subsequent to surgical removal or resection of the tumor.

15. (Original) The method according to claim 1, wherein the partially matured dendritic cells are administered to a tissue area surrounding the tumor.

16. (Original) The method according to claim 1, wherein the partially matured dendritic cells are administered into a lymph node directly draining a tumor area.

17. (Original) The method according to claim 1, wherein partially matured dendritic cells are administered directly to a circulatory vessel duct that delivers blood or lymph to the tumor or a tumor afflicted organ.

18. (Original) The method according to claim 1, wherein the partially matured dendritic cells are administered into the circulatory system such that the cells are delivered to the tumor or tumor afflicted organ.

The teaching of Triozzi et al and Labeur et al has been set forth above.

Triozzi et al and Labeur et al do not teach DCs are administered directly into the tumor, to a tissue area surrounding the tumor, into a lymph node directly draining a tumor area, directly to a circulatory vessel duct that delivers blood or lymph to the tumor or a tumor afflicted organ, or into the circulatory system such that the cells are delivered to the tumor or tumor afflicted organ.

Labeur et al further teach that subcutaneous injection is not the optimal cell delivery system for in vitro generated DCs, at least in the mice, because DCs migrate very **inefficiently** into the regional lymph nodes after subcutaneous injection into mice (p.171, second column, last paragraph, bridging p.172, p.174, second column, last paragraph).

It would have been prima facia obvious for one of ordinary skill in the art at the time the invention was made to administer DCs taught by Triozzi et al and Labeur et al to a tissue area surrounding the tumor, into a lymph node directly draining a tumor area, directly to a circulatory vessel duct that delivers blood or lymph to the tumor or a tumor afflicted organ, or into the circulatory system such that the cells are delivered to the tumor or tumor afflicted organ, to increase the number of available sites for DCs injection, from which DCs could be readily delivered to the tumor, in view that DCs migrate very inefficiently into the regional lymph nodes after subcutaneous injection into mice, as taught by Labeur et al.

4. Claims 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07 in view of Labeur et al, 1999, J Immunol, 162: 168-175, and further in view of Nikitina et al, 2001, Int J Cancer, 94: 825-833, IDS# AN of 05/09/07.

Claims 19-20 are as follows:

19. (Original) The method according to claim 1, wherein the partially matured dendritic cells are administered as an adjuvant to radiation therapy, chemotherapy, or combinations thereof.

20. (Original) The method according to claim 19, wherein the partially matured dendritic cells are administered prior to, simultaneous with, or subsequent to radiation therapy, chemotherapy, or combinations thereof.

The teaching of Triozzi et al and Labeur et al has been set forth above.

Triozzi et al and Labeur et al do not teach that DCs are administered as an adjuvant to radiation therapy, chemotherapy, or combinations thereof. Triozzi et al and Labeur et al do not teach that the partially matured dendritic cells are administered prior to, simultaneous with, or subsequent to radiation therapy, chemotherapy, or combinations thereof.

Nikitina et al teach that gamma **irradiation** induces the dramatic ability of DCs injected i.v. or s.c. to migrate and penetrate cancer tissue, and to take up apoptotic bodies, resulting in enhanced, potent antitumor response (abstract, p.831, second column, last paragraph bridging p.382).

It would have been prima facia obvious for one of ordinary skill in the art at the time the invention was made to combine DCs administration taught by Triozzi et al and Labeur et al with radiation therapy, because gamma irradiation induces the dramatic ability of DCs injected i.v. or s.c. to migrate and penetrate cancer tissue, and to take up apoptotic bodies, resulting in enhanced, potent antitumor response, as taught by Nikitina et al.

5. Claims 21-23, 25, 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07, in view of Labeur et al, 1999, J Immunol, 162: 168-175, of record, and Sukhatme et al (US 6,797,488).

Claims 21-23, 25, 27-32 are as follows:

21. (Currently amended) A composition comprising partially mature dendritic cells combined with a pharmaceutically acceptable carrier for in vivo administration, wherein the partially mature dendritic cells have been contacted in vitro with a dendritic cell maturation agent.

22. (Original) The composition according to claim 21, wherein the partially mature dendritic cells demonstrate an up-regulation of co-stimulatory molecules CD80, CD86 and/or CD54 and retain the ability to uptake and process antigen.

23. (Original) The composition according to claim 21, wherein the composition comprises about 10^2 to about 10^{10} partially matured dendritic cells.

25. (Original) The composition according to claim 21, wherein the partially matured dendritic cells have been isolated from a patient to whom they are to be administered.

27. (Original) The composition according to claim 21, wherein the partially matured dendritic cells are administered directly into the tumor.

28. (Original) The composition according to claim 21, wherein the partially matured dendritic cells are administered into a tumor bed subsequent to surgical removal or resection of the tumor.

29. (Original) The composition according to claim 21, wherein the partially matured dendritic cells are administered to an tissue area surrounding the tumor.

30. (Original) The composition according to claim 21, wherein the partially matured dendritic cells are administered into a lymph node directly draining a tumor area.

31. (Original) The composition according to claim 21, wherein partially matured dendritic cells are administered directly to a circulatory vessel duct that delivers blood or lymph to the tumor, tumor bed, or a tumor afflicted organ.

32. (Currently amended) The composition according to claim 21, wherein the partially matured dendritic cells are administered into the circulatory system such that the cells are delivered to the tumor, tumor bed, or tumor afflicted organ.

Claims 21-23, 25, 27-32 recite the claimed composition for administering: 1) in vivo, directly into the tumor, 2) into a tumor bed subsequent to surgical removal or resection of the tumor, 3) to an tissue area surrounding the tumor, 4) into a lymph node directly draining a tumor area, 4) to a circulatory vessel duct that delivers blood or lymph to the tumor, tumor bed, or a tumor afflicted organ, or 5) into the circulatory system such that the cells are delivered to the tumor, tumor bed, or tumor afflicted organ. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims 21-23, 25, 27-32 read on the ingredient per se, which is a composition comprising dendritic cells partially matured in vitro.

The teaching of Triozzi et al and Labeur et al has been set forth above. Triozzi et al further teach that DCs generated in vitro by GM-CSF and IL-4 express the co-stimulatory molecules **CD80 and CD86**, and a low number of CD83 (p.2649, first column, item under Results). Triozzi et al teach that the amount of DCs generated is from 8.0×10^7 to 18×10^7

(p.2649, first column, item under Results). The amount of DCs taught by Triozzi et al is within the range of the claimed amount of DCs, as claimed in claim 23.

Triozzi et al and Labeur et al do not teach DCs in a pharmaceutically acceptable carrier.

Sukhatme et al (US 6,797,488) teach an anti-angiogenic protein, fusion protein thereof (column 2, item under Summary of the invention, bridging column 3), and a composition thereof, wherein the protein is combined with a **pharmaceutically acceptable carrier** (column 16, last paragraph, bridging column 17).

Although the Triozzi reference does not explicitly teach that the generated DCs are partially mature, however, the claimed DCs appear to be the same as the prior art DCs, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the DCs taught by Triozzi et al and Labeur et al with a pharmaceutically acceptable carrier, as taught by Sukhatme et al, for their storage.

7. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Triozzi et al, 2000, Cancer, 89: 2646-54, IDS# AU of 05/09/07, in view of Labeur et al, 1999, J Immunol, 162: 168-175, of record, and Murphy et al (US 5,788,963, filed on 07/31/1995), of record.

26. (Original) The composition according to claim 21, wherein the partially matured dendritic cells have been HLA matched to an individual to whom they are to be administered.

The teaching of Triozzi et al and Labeur et al has been set forth above.

Triozzi et al and Labeur et al do not teach that the generated DCs have been isolated from a healthy individual HLA-matched to the individual to be treated.

Murphy et al teach that DCs can be obtained from prostate **cancer patient to be treated, or from healthy individual with matched HLA** in terms of HLA antigens, because patients previously treated radiation or chemotherapy often are not able to provide sufficient or effecient DCs (column 6, lines 37-57). Murphy et al teach that CD8+ T cells, after interaction with antigen presenting cells, which express MHC class I or II molecule associated with the antigen, are sensitized and capable of killing any cells that express the specific antigen associated with matching MHC class I molecule (column 2, second paragraph). It is noted that DCs are antigen presenting cells.

It would have been obvious that to replace DCs obtained from the individual to be treated taught by Triozzi et al and Labeur et al with DCs that have been isolated from from a healthy individual HLA-matched to the individual to be treated, as taught by Murphy et al, to increase the number of available DCs, for example, in situations where the patient to be treated cannot provide sufficient DCs, as taught by Murphy et al. Further, an HLA-matched DCs would be

necessary, because antigen presentation of DCs is restricted to the complementing HLA molecule, in view of the teaching of Murphy et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS

February 5, 2009

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643